Claims 2-7 on the ground of non-statutory obviousness-type double patenting over claims 12-13 of Kitazawa in view of Yamagishi and Williamson.

The above rejections are respectfully traversed.

Applicants focus on the rejection of claim 1, the Examiner's criticism of the DECLARATION evidence and the basic flaw in the Examiner's reasoning.

Summarizing the rejection, Applicants have submitted DECLARATION evidence. The Examiner admits that the DECLARATION establishes that Yamagishi and Kitazawa generate the β form, not the α form which is claimed herein. Applicants and the Examiner are in agreement on that point. However, the Examiner continues and concludes that an obviousness rejection is proper because there was no attempt to modify the Yamagishi and Kitazawa procedures following the "guidance" of Williamson.

Applicants respectfully submit that the error in the Examiner's basic reasoning is that since the art was unaware of the fact that the crystals of the present invention exist in the α and β form, there would be no motivation to vary in any fashion from the teaching of Yamagishi or Kitazawa to use the Williamson procedure. Since the α form was not known to exist, there would be no motivation for one of ordinary skill in the art to modify Yamagishi or Kitazawa which teach, according to that prior art, perfectly acceptable procedures for generating the form of the crystals obtained therein, namely the β form.

However, Applicants offer the following additional comments on the rejection. They rely upon the arguments below to traverse both the obviousness and double patenting rejections.

It is known that crystalline polymorphism may be caused not only by the re-crystallizing solvent but also by factors such as the cooling method (temperature, speed, cooling medium), the crystallization temperature, the supersaturation degree, the agitation speed, the seeding method (timing, temperature, amount) and any impurity (character (organic, inorganic), property and amount).

Since any of the above factors can lead to obtaining different crystalline forms, if one of the above factors differs, even if the same recrystallization solvent is used, one may not obtain the same crystalline form. This factor is important in interpreting the value of Williamson.

Williamson merely teaches known steps of crystallization, and teaches as follows regarding crystallizing a solute as follows.

(a) The crystallization process should normally start from a solution that is saturated with the solute at the boiling point.

(b) Once it has been ascertained that the hot solution is saturated with the compound just below the boiling point of the solvent, it should be allowed to cool slowly to room temperature.

(c) Adding a seed crystal or scratching the inside of the tube containing (b) with a glass rod at the liquid-air interface will initiate crystallization.

(d) Once it is seen that crystallization has started, the solution must be slowly cooled without disturbing the container in order that large crystals can form.

(e) Once the tube has cooled to room temperature without disturbance, it can be cooled in ice to maximize the amount of product that comes out of solution.

Simply stated, Williamson merely teaches basic crystallization procedures and neither discloses nor suggests in any fashion obtaining crystalline polymorphs, and in no fashion teaches factors which cause or result in crystalline polymorphs and how to control crystallization procedures to obtain different polymorphs.

Thus, Williamson does not provide motivation for one of ordinary skill in the art to modify Yamagishi or Kitazawa. Yamagishi and Kitazawa teach, on their face, perfectly acceptable crystallization procedures. Neither reference teaches there is an α form and a β form. Lacking knowledge of the α form or the β form, one of ordinary skill in the art would not have any reason to modify Yamagishi or Kitazawa according to Williamson, except the knowledge provided by the present application that there is, in fact, there is an α form and β form.

As is clear from the record, the method for the production of crude crystals of Yamagishi differs from that of the present invention. Therefore, it is quite logical to conclude that one of the factors earlier discussed as affecting crystalline polymorphism exists, most probably an impurity contained in the crude crystals of Yamagishi differing from that of the present invention. Thus, the procedure of Yamagishi is very different from the procedure of the present invention with respect to some factor other than the crystallization process, i.e., a factor which would not be affected if Yamagishi were modified by Williamson.

Similar remarks would also apply to Kitazawa.

Applicants thus respectfully submit, considering the record they have built, that one of ordinary skill in the art would have no motivation to modify the procedure of Yamagishi or Kitazawa in view of Williamson to reach the unknown α form of the present invention.

Withdrawal of all rejections and allowance is requested.

Interview Summary

A telephone interview was conducted concerning this application.

Yamagishi and Kitazawa were discussed in general and the emphasis was on Williamson. The Examiner expressed the view that one of ordinary skill in the art would be lead to modify Yamagishi and/or Kitazawa in view of Williamson. The Examiner's basic point, as reflected in the present Action, was whether the α form would be obtained if Yamagishi and Kitazawa were modified per Williamson. The undersigned indicated that this point would be explored with the Inventors.

A rather unusual turn during the interview was that the Examiner raised concern that the α form might have been used in clinical trials and would create a statutory bar. Applicants have the following comments thereon.

Clinical trails are performed as follows:

When drugs for clinical trials are manufactured by a third party, manufacture is performed under a secrecy agreement.

The clinical trials are performed at a restricted hospital(s) under a secrecy agreement.

The drugs for the clinical trials are strictly controlled so that doctors, nurses, patients and others do not know the identity of the drug and the method of manufacturing the same is not known.

Accordingly, in Applicants view, whether clinical trials are performed in the United States or elsewhere, the clinical trials would not create prior art under 35 U.S.C. § 102(a) or (b).

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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23373
CUSTOMER NUMBER

Date: October 27, 2006